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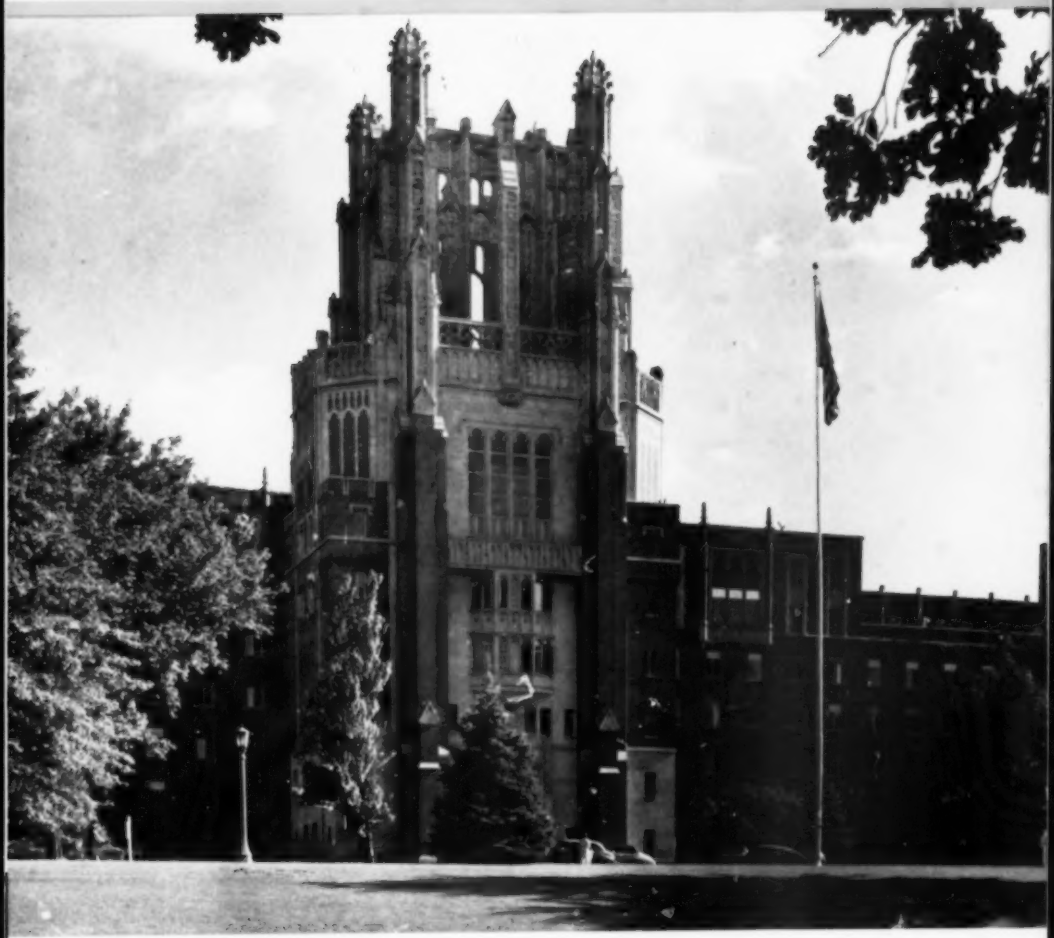

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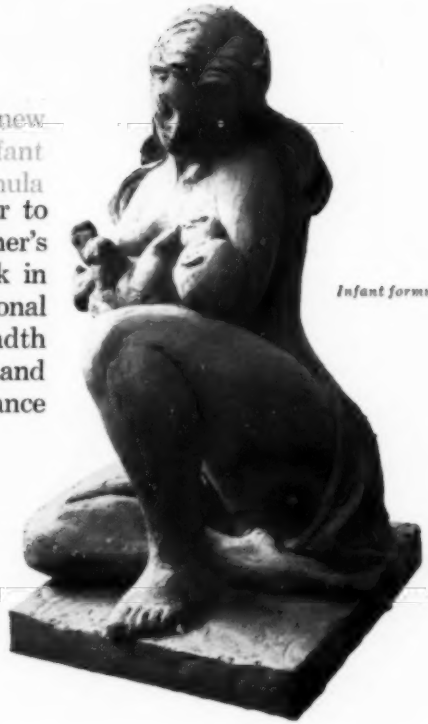

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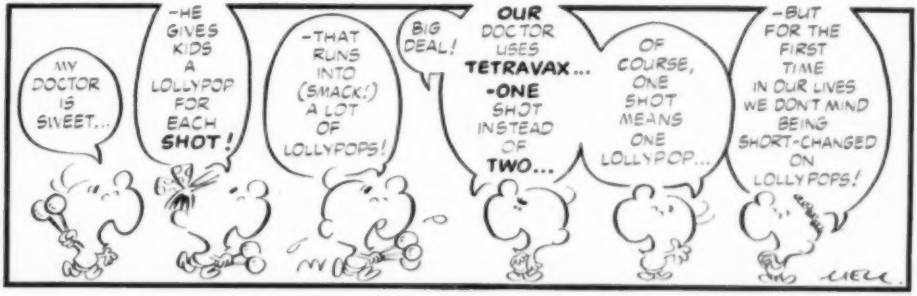

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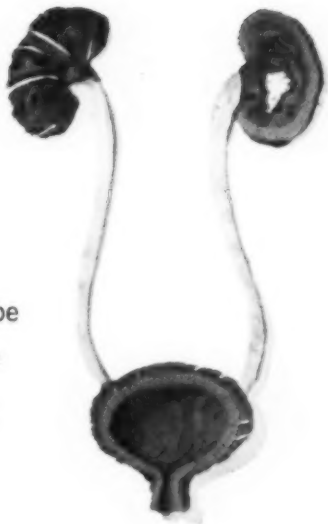

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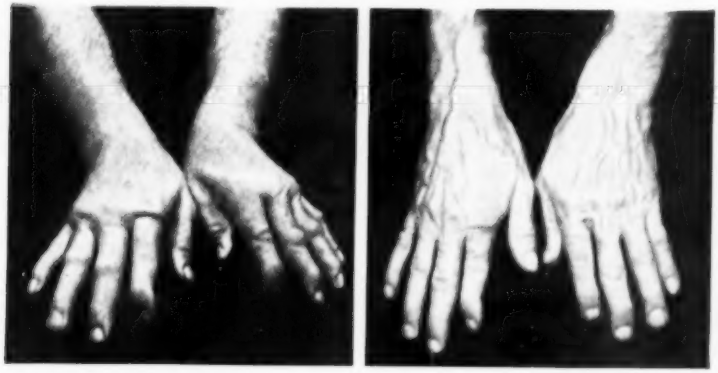

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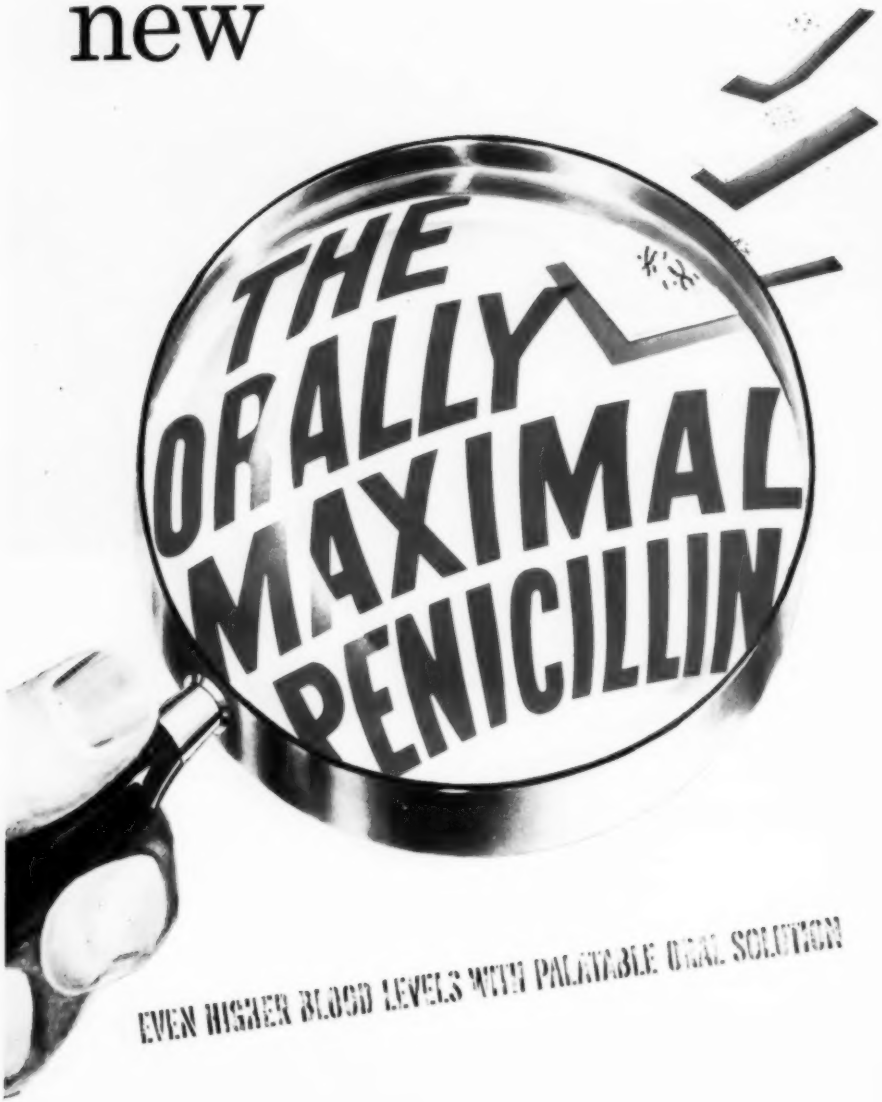

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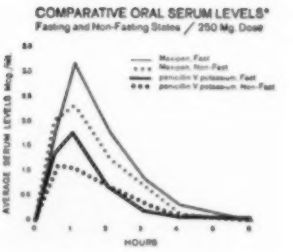

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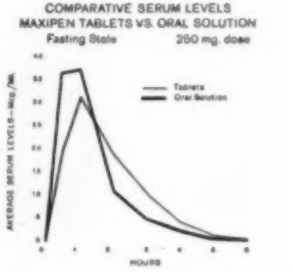

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guest editorials

Deafness From Mumps

KEEP IT IN MIND

EDMUND PRINCE FOWLER, M.D.*
New York

DEAFNESS caused by mumps is well known and Lindsay has described its inner ear lesions.[1] Unfortunately over the ages mumps in children has been taken somewhat in a casual manner, usually almost as a joke, in spite of its sometimes serious complications, such as involvement of the testes, ovaries, breasts, other glandular organs and rarely the neural tissues, peripheral and central. When the swelling presses sufficiently hard on the 7th nerve, facial paralysis results.

Herein we wish to dwell upon one of its serious consequences, its threat to the hearing.

It is quite obvious that infectious perotitis is a spotty, systemic disease of the body, although it may and often does apparently affect only one parotid gland. Its symptoms may be severe or so trivial that they are not noticed either by the child or his parents.

During our wars it has been observed that although there was frequently no history of mumps in recruits coming from the larger cities these men seldom contracted mumps whereas the country boys with no history of mumps came down with the disease in large numbers when an epidemic of mumps occurred. The reason for this discrepancy in susceptibility was that many of the city boys presumably had previously acquired immunity by an attack of mumps which may have been so mild that it was not diagnosed, or had been forgotten.

It is evident that pediatricians should alert mothers and nurses to the possibility of mumps deafness and caution them to test the child every day for two weeks after the onset of mumps. This probably can be most easily done by having the child listen to the ticking of a watch held near one of his ears tightly closing, first one and then the other opposite ear, by pressing firmly on the tragus of each with the finger.

*Chairman, Subcommittee on the Hard of Hearing and the Deaf of the Council Committee on Public Health and Education of the Medical Society of the State of New York.

Unfortunately the mildness of an attack of parotitis does not preclude serious involvement of other organs and especially the ear. Unrecognized mumps can cause severe deafness, frequently even total deafness. Fortunately this deafness usually affects only one ear and has been considered to be irreversable.

When we observe sudden deafness from mumps and it is accompanied by severe vertigo and maybe even nausea and vomitting it indicates that the entire otic labryinth is then involved. However, in the little child these signs may be misinterpreted or unobserved, even though present, because the child is sick, maybe very miserable in bed, and does not describe his symptoms to the parents, nurse or doctor, and if his eyes are closed any nystagmus that is present can be observed only by careful observation of the movement of the eyeballs beneath the closed lids. When the mumps subsides the child although totally deaf in one ear, may not be aware of the deafness or mention it for several years, long after the mumps has become a dim memory.

Only a small minority of people with mumps deafness give a history of vertigo, indicating that the vestibular labyrinth is often not much if at all affected in such cases. Although the virus travels by way of he blood and would be expected to reach all parts of the body often no symptoms of damage to other parts of the body appear. Why it usually does not do more damage and especially to the closely coupled endolymph filled channels in the inner ear is a mystery.

The lesions seen microscopically in the case recently reported by Lindsay[1] showed the stria vascularis in the scala media moderately involved and as with Corti's organ there was more pathology in the basal and less and less in the middle and upper turns. Some sections revealed a complete inward collapse of Reissner's membrane so that it lay against the basilar membrane and its degenerated hair cells.

It seems probable that the spotiness of the lesion in mumps is due to vascular phenomena which of course occur with practically all disease. I am referring to the white and red clumps of cells which have variously been called red or white aggregates, platelet aggregates, or as suggested by Knisely, "blood sludge." In 1950 I suggested that sudden deafness[3] could be caused by plugging of the vessels in the membranous labyrinth by intravascular clumping of the blood. In 1958 my son, Edmund Jr., discussed these pheno-

mena before the Eastern Section of the American L. R. & O. Society.[2] All viral and bacterial poisons act not only per se, but by causing intravascular clumping they can secondarily damage tissues, particularly delicate neural tissues. If a blockage of a blood vessel is sufficiently prolonged a local anoxia occurs which can suffocate the cells and reduce or destroy function.

Consider the fact that even two red blood cells stuck together face to face cause 50% loss of exposure of their surfaces and ten cells so stacked smother 90% of the surfaces. In general the larger the masses the slower the blood flow and the greater the degree of anoxia in the tissues affected.[3] Blocking of the auditory artery by a white or red embolus or thrombus caused by mumps virus would explain the pattern of the disease and probably the fact that the disease is usually unilateral.

If the masses are large and sufficiently firm they can not easily get into the smaller vessels, the arterioles, but can easily get into and block the larger channels and deprive the blood in their branches of oxygen and other metabolites. The circulation in the membranous labyrinth is terminal; there is no collateral circulation. We should keep in mind that the vascular channels to the basal turn of the cochlea are generally longer and larger than those to the upper turns, and therefore are more patent to larger masses than the smaller channels in the upper turns.

Vascular agglutination blocking the auditory artery, or even more probably, blocking the venules of the stria vascularius could easily occur in mumps since we know that 40% or more of victims of mumps have a pleocytosis in the spinal fluid indicating some form of meningo encephalitis. This is in spite of the fact that very few patients show symptoms of meningo encephalitis. However, since relatively few patients with clear cut meningo encephalitis have any deafness there must be another factor. Therefore my son and I bring up the idea that the vascular factors are the culprits that precipitate the deafness.

If this is so, a line of treatment becomes apparent. It is known that intravascular agglutinates can be influenced by heparin and that heparin is an anti inflammatory agent.[4]

Although it is thought that it is dangerous to use heparin with little children it has been used without harm, and I suggest that it be tried in cases of mumps deafness which have been detected early.

There are several other drugs which may be tried, for example nicotinic acid. Recently in two cases my son has used it and the hearing did not become total following a loss attributed to mumps. Also intravascular procaine was used on the elder of these two children who was treated within 30 hours of the onset of his hearing loss. This drug increases the rate of blood flow and has been successfully used in sudden deafness in Meniere's disease.[2] Especially as an emergency measure I favor nitroglycerine under the tongue because it acts more quickly than nicotinic acid.

Remember when sudden deafness occurs we are faced with an emergency; with a calamity, and quick, bold action is indicated.

Incidentally relief from severe pain lessens neuro-vascular repercussions which can and often do increase the formation and prolongation of the aggregating phenomena. It is pertinent to mention the fact that cold packs reduce swelling of the parotid and surrounding tissues which swelling and edema aside from the threat to the facial nerve, if severe or prolonged, may by slowing the circulation favor the formation of intravascular agglutination of the blood.

In any event let us not continue to ignore the threat of severe or total deafness from mumps. Let us always be on the alert to forestall it and possibly to relieve it by prompt measures along the lines I have suggested or by other measures which will without doubt be available as our understanding of the lesions improves.

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Psychoneurological Learning Disorders in Children

Helmer R. Myklebust, Ed.D.*
Benjamin Boshes, M.D.*
Illinois

Perhaps there is no more important effort in science than the study of learning, inasmuch as it entails all aspects of Man's behavior, normal and abnormal. Historically such study was mainly concerned with the relative importance of heredity and environment. Much progress was made in understanding the learning process through this "heredity-environment" controversy. Currently the emphasis is more dynamic, less either-or, with vital interest in the variables and variations which occur. There is a basic curiosity with the ways in which the influences of either heredity or environment might be demonstrated, curtailed or modified.

Frequently the psychiatrist, neurologist, psychologist and educator are confronted with a need to understand impositions and deterrents to learning. This need might arise through the case of a child who is not learning to talk, or not learning in other ways according to the demands of the society in which he lives. Perhaps the inquiry arises through an adult who, because of a vascular accident, has lost a specific aspect of his learned behavior, such as the ability to learn to read; now this adult must attempt to re-learn that which he lost. Another type of problem, growing in importance, is the need to understand the effects of drugs on learning. Clinically it seems that a drug which is effective in the treatment of a disease such as epilepsy might also be an imposition to learning.

Learning can be affected in many ways. It is advantageous scientifically to classify factors that impair learning into three major categories; those which have a psychological causation, those caused by impairment of the peripheral nervous system, and those due to disorders of the central nervous system. This is shown schematically in Figure One.

* From the Institute for Language Disorders and the Department of Neurology and Psychiatry, Northwestern University, Evanston-Chicago. The authors acknowledge assistance from Doris Johnson, Arthur Neyhus, Katherine Poole, Ellen Spencer, Joel Brumlik and Hirsh Wachs.

FIGURE 1

Primary Deterrents to Learning

Affective Disorders	*Peripheral Nervous System Disorders*	*Central Nervous System Disorders*
Neuroses	Deafness	Perceptual Defects
Psychoses	Blindness	Language Disorders

Affective disorders have been emphasized a great deal in the past few decades, especially in the United States. Conceivably this emphasis has obscured other significant deterrents to learning. The effects of sensory impairments also have been stressed. More recently other factors which impede learning have come into the foreground. These involve the neurology of learning and can be referred to as *psychoneurological learning disorders.* Such aberrations of the learning process are not explicable on the basis of emotional disturbance, or sensory impairment, although superficially both of these factors often seem to be the etiology.

Psychoneurological learning disorders are those which derive from neurological maladies. It has been recognized that a neurological involvement can cause cerebral palsy and mental deficiency. We are less cognizant that minor motor incoordinations, certain behavior disturbances, disorders in reading, writing, spelling, arithmetic, and speaking might have a neurological causation. The central nervous system involvement may be slight and even inconsequential neurologically, but frequently the effect on learning is marked. It must be emphasized that the term *psychoneurological* includes only those psychological, behavioral deviations which are attributed to neurological causation. While in this paper we are concerned with the psychoneurological disorders in children, this classification might include any psychological deviation resulting from brain disorder. For example, the aphasias, dyslexias, and memory defects which result from brain diseases in middle age, and the deficits of behavior which occur geriatrically, can be viewed as being psychoneurological in nature.

Terms such as "brain-damaged" and "brain-injured" have been used to designate certain children presenting problems of behavior and learning. These terms have marked limitations both clinically and scientifically. The disorder might be due to endogenous, or mal development factors, rather than damage or injury per se. The term *psychoneurological* can be used for all aberrations of

behavior which have a neurological basis, irrespective of age of onset and etiology. This term also has the advantage of being less traumatizing and stigmatizing. Psychoneurological disorders may occur in children and adults who otherwise are of average or above intelligence. Moreover, they may be found in individuals who seem to be intact neurologically. It should not be inferred that neurological involvements cannot be demonstrated. On the contrary, research is revealing a high correlation between certain disorders in children and minimal neurological conditions.

Our major purpose here is to accent psychoneurological learning disorders which are congenital in origin. In Blakiston's New Gould Medical Dictionary, *congenital* is defined as "existing at birth". It is in this sense that we use the term. Hence we assume that if the condition is congenital in origin, it was caused either prenatally or during birth. For example, the neurological involvement might have been caused prenatally by maternal rubella, or by anoxia associated with atypical factors at the time of birth. However, although the neurological ailment is congenital, the concomitant learning disorder does not become apparent except through the later development of the child; perhaps at the age when he *should* be talking, dressing himself, or learning to read. The following discussion describes some common learning disorders in children, with case illustrations.

CONGENITAL APRAXIA

Apraxia is the inability to ideationally plan a motor act. It is the inability to relate specific experience to the appropriate motor system when there is no paralysis and when the condition derives from neurological disorder. Although an apraxia may be generalized, perhaps one of the best known apraxic involvements is that which occurs in expressive aphasia. The individual knows the word he wishes to say but cannot relate the *symbol* and the motor system for speaking. Apraxia is a defect in expressive function as contrasted with receptive function; it is an output disorder, not an input disorder. Congenital apraxia, especially in the form of *expressive aphasia*, seems to be more common than has been assumed; it is a common type of psychoneurological learning disorder in children. This condition in children symptomatically often is highly similar to that seen in adults. Another type of apraxia seen less frequently in children is *dysgraphia;* the inability to "think" the motor plan for writing because of neurological disorder, but without paralysis being involved.

CASE ONE: EXPRESSIVE APHASIA

This boy, 4 years and 2 months of age, was referred by a pediatrician. The history revealed complications during pregnancy because of "structural" involvements. Etiology is obscure with a possibility of prenatal anoxia.

Psychological study and evaluation of language revealed normal intelligence (I.Q. 107) with expressive aphasia, dysarthria, visuo-motor disturbance, and a formulation disability. He related to people and used gestures freely in making himself understood.

The neurological examination revealed minimal but definite signs of central nervous system disturbance. Both pyramidal and extra pyramidal systems were involved, the greater evidence on the right side of the body. The EEG was abnormal, a generalized slow record with mild asymmetrical slow waves in the left frontal, left temporal, left parietal, right parietal and right temporal areas.

He was started on language and educational therapy which continued for 2 years. He is now 6 years of age and is in a regular first grade in public school without need for additional specialized training.

CONGENITAL AGNOSIA

An agnosia is an input disorder, not an output disorder. Hence this defect relates to the primary sensory channels in Man; visual agnosia, auditory agnosia, and tactual agnosia. Agnosia means a "lack of knowing". It is the inability to interpret, that is, to associate meaning with the sensations being received. Like apraxia, this condition might entail both symbolic and non-symbolic aspects of behavior. For example, an auditory agnosic might be unable to interpret any sound, or just be unable to interpret the spoken word. Again, it is agnosia for verbal symbols which is most readily recognized and clearly understood clinically. When the auditory agnosia involves the ability to comprehend the spoken word it is referred to as a *receptive aphasia*. If the visual agnosia entails comprehension of the written word it is referred to as *dyslexia*. *Tactual agnosia* is more difficult to determine, especially in children. Interestingly it is more readily recognized in blind children because of their need to use the tactual sense symbolically in learning to read Braille. If the agnosia entails either the auditory or visual aspects of number ability it is referred to as *dyscalculia*.

As the above discussion has inferred, the most commonly recognized psychoneurological learning disorders in children pertain to the acquisition and use of language. This manifests itself frequently through children who do not learn to speak, to read or to write. In this connection it is helpful to keep in mind that "output" is dependent on "input". Thus, the child will not speak until he has minimal comprehension established, and he will not write until he has established minimal ability to read. As would be expected, it is the receptive disorders which are the most debilitating behaviorally. The child who cannot learn to comprehend the spoken word is more seriously deficient in relation to his environment than the child who cannot get the words out. Another consideration is that the involvements of the brain affecting areas for reception, as contrasted with areas for expression, may be more basic to the total integration of the individual.

A survey which we made of psychoneurological learning problems in children, indicated that the most common language disorder found in public school children is dyslexia. Although there has been some resistance to the term congenital aphasia, the term *congenital dyslexia* has been used widely both in the United States and in Europe. While, like all language disorders, it is a complex problem, usually the child is either unable to learn what the letters look like, or to learn what sounds go with the letters. In other words, dyslexia might result mainly from defects in visual associations or from defects in auditory associations. At times both auditory and visual associations are involved. Often a genetic, endogenous factor is indicated. This has been especially emphasized in Sweden. In our studies, even though endogenous factors are indicated, neurological disturbances usually can be demonstrated.

The concepts of *re-visualization* and *re-auditorization* are highly useful in the study of learning disorders in children. This is shown most clearly through the child's learning to write. Evidence indicates that the child cannot learn to spell or to write, unless he can simultaneously *revisualize* what the letters look like and *reauditorize* what the letters sound like. The implications of such findings for training and educational therapy are manifold and cannot be discussed here. This criterion is helpful in distinguishing between the child who is truly dysgraphic and the one who cannot write because of defects in revisualization or reauditorization. Furthermore it can be used in differentiating between children who have expressive versus receptive aphasias.

CASE TWO: RECEPTIVE APHASIA

This boy was seen first when he was 5 years and 4 months of age. The parents requested a conference because of his inability to comprehend what was said to him. The history disclosed an Rh factor with jaundice after transfusion. Severe convulsions were present for over two years. When first seen he was distractible auditorially. Sounds provoked marked anxiety and hyperactivity. He related to people only to a minor extent, and superficially.

Study revealed a receptive aphasia with echolalia and a marked disturbance of auditory perception. Initially mental capacity could not be established because of extreme scatter of abilities. He was judged clinically to have at least low average mental ability and this has been verified recently when he earned an I.Q. of 80 on the Performance Section of the Wechsler Intelligence Scale for Children.

Neurological examination disclosed minimal evidence of central nervous system dysfunction. The EEG study showed mild dysrhythmic slowing, mainly in the frontal lobes bilaterally. Drug therapy was inaugurated and has prevented seizures.

Educational language therapy has been in progress for almost three years. He has learned to tolerate stimulation well in a structured environment. As his comprehension has improved, his ability to relate with both children and adults has increased. Progress in learning has been excellent and is continuing. He is now approaching 8 years of age. He is in a regular public school class with a group one year younger than himself, and specialized language therapy is continuing. The outlook is good for self-support and adjustment in society.

CASE THREE: DYSLEXIA

Characteristic of dyslexics, this boy's inability to read and his school failure have been attributed to various causations. When first seen by us he was 15 years and 3 months of age. The history revealed very difficult labor with possible anoxia at the time of birth. Total evaluation of capacities and learning disorders revealed a dyslexia with difficulties in revisualization and reauditorization, a spelling defect, dysmonia, a deficiency in time-sense and a memory disturbance. Level of mental capacity ranged from average to above average with scores clustering from 90 to 110.

He was referred for neurological examination and found to have minimal neurological signs pointing to a right pyramidal tract lesion. The EEG was mildly abnormal consisting of left occipital scattered slowing, spreading to the right occipital area in the waking state. In this case the psychological findings and the EEG findings are strikingly corroborative.

After 15 months of therapy covering reading, spelling, memory, and other aspects of his learning disorders, he is making good progress. He is in a public high school but receives supplemental educational therapy at the Institute for Language Disorders. At the outset of his training he used many defense mechanisms in attempts to conceal his deficits in learning. He now verbalizes problems which are difficult for him and tries to overcome them. He has excellent motivation and relates well both to his own and peer groups.

CASE FOUR: DYSCALCULIA

This boy was first seen at the age of 4 years and 8 months. He presented problems in behavior, poor speech and language development. He was studied over a period of time because of the difficulty of obtaining objective evidence of mental capacity. Through language therapy and guidance of the parents behavior improved. Recently on objective tests of mental ability he scored at least at 100 I.Q. There is now no question about his *ability* to learn.

The only suggestion of etiology from the history is the possibility of anoxia at the time of birth. Inclusive evaluation of behavior and learning revealed a mild expressive aphasia and dysarthria, with dyslexia and a marked dyscalculia.

Neurologically there were mild but definite signs indicating either bilateral cerebral disease involving the pyramidal tracts of both sides, or a lesion in the brain stem in the region of the decussation of the pyramids; the former seemed the most probable. The EEG was mildly abnormal, consisting of slow waves in the biparietal areas, occasionally becoming generalized. Slow waves were observed in the right frontal and right occipital areas more prominently than elsewhere.

This lad has had unusually difficult learning problems. We have now worked with him in educational therapy for approximately 6 years. He no longer has significant aphasia or dysarthria. Furthermore, dyslexia is no longer a handicap, although the dyscal-

culia continues to some extent. Interestingly, he can calculate exceedingly well when told to add, multiply or divide. But he has marked difficulty in ascertaining which of these processes is appropriate when he is confronted with an arithmetic problem.

TOPOGRAPHIC ABILITY, ORIENTATION AND TIME

Psychoneurological learning disorders in children are not limited to language. *Topographic defects* commonly are seen in association with dyslexia. In this condition the inability is one of not being able to associate experience with maps, globes, and other representations of space. *Orientation disturbances* are seen most often as confusions of left and right, and in learning directions. *Time disorders* may include learning to tell time by a clock, learning the days of the week, months and seasons of the year, and many other time relationships.

CASE FIVE: ORIENTATION AND TIME DISORDER

A boy, 7 years of age, was seen because of his inabilities in learning. Study of psychological factors disclosed visual and auditory perceptual problems with minor residual receptive and expressive aphasia. In addition there was a *marked time and left-right disorientation*. Mental capacity fell within the normal range.

Neurological appraisal showed minimal evidences of dysfunction, with the left hemisphere most involved. The EEG was mildly abnormal with slowing in the left-parietal-occipital area in hyperventilation; perhaps some loss of voltage and fusion of waves in the right occipital area in sleep.

Etiology was obscure, with possible anoxia. This child is in the first grade in a public school and presenting serious problems in learning. He is in need of program planning.

IMPLICATIONS OF PSYCHONEUROLOGICAL LEARNING DISORDERS

A psychoneurological learning disorder in a child has important, sometimes urgent implications. It might be a forewarning of epilepsy. In certain instances there are implications for the presence of progressive diseases such as hydrocephalus, tumors or Heller's disease.

There are other types of implications. These disorders are found in otherwise bright, even brilliant children. For all children having psychoneurological problems specialized training and therapy are needed if their needs are to be met, if they are to have an opportunity for actualization of their potential. Problems of emotional overlay are common. The parents require assistance in

understanding the total needs of the child, the neurological involvements as well as the learning disturbances, which entail a long period of remedial therapy.

Specialized educational training is of critical importance. Because language disorders are encountered so frequently this is an important part of any such program. The area concerned with the scientific study of disturbances of language behavior is referred to as *language pathology*. Knowledge in this area is growing. From research and clinical experience it is increasingly apparent that much can be done to alleviate and modify learning disorders. However, outcomes are related to early diagnosis and therapy. Unfortunately it is common to see children whose psychoneurological problem is recognized only after years of school failure, usually preceded by erroneous diagnosis. We frequently see young adults in high school, and at times even in college, whose learning disorders predated entrance to kindergarten. Proper study often indicates that the onset was prenatal. Through therapy procedures which are firmly based on specific diagnostic findings the child usually can be helped substantially. Each child must be viewed individually, according to his total matrix of disturbances, with a program planned to cover both the medical and learning involvements. When this is done the prognosis is good for independent adjustment in society.

RESEARCH

There is an urgent need for research on psychoneurological problems at all age levels, with children and adults. Our studies covering a period of approximately ten years have pertained principally to children. An extensive research project has been in progress for three years and will continue for the next five years. Children presenting problems in learning are first studied behaviorally to determine that intelligence is normal, that sensory capacities are intact, and to define the type of learning disorders present. Secondly, the child receives neurological and electroencephalographic study. Total time devoted to the examination of each child is from eight to ten hours. All findings, neurologic, electroencephalographic and behavioral are coded and treated statistically through the use of an IBM electronic computer. While it is premature to present statistical findings, some generalizations can be made:

(1) A survey of a public school population indicated that the number of children having psychoneurological learning disorders might exceed 5 per cent.

(2) The incidence of these disorders is at least five times more common in males than in females.

(3) A preponderance of the children who present problems of revisualization have disturbances in the occipital-parietal area.

(4) A highly significant number of children who present problems of reauditorization have disturbances in the temporal-parietal area.

(5) Because there is a relationship between neurological findings and learning disorders, there are indications that in the future the neurologist will be able to predict such disorders from his studies.

(6) Certain psychometric procedures indicate not only the presence of learning disorders, but the area of the brain which is involved.

(7) Educational-language therapy procedures can be planned according to the specific type of psychoneurological problem existing; this provides a scientifically oriented therapy program.

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A New Sedation for Electroencephalograms of Disturbed Children in a General Hospital*

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This discussion represents a three-year study of the usefulness of the drug, BULBOCAPNINE, in the management of difficult patients whose records would, most probably, have been poor or valueless without the assistance of the drug. As an EEG laboratory in a general hospital with an unusually large number of patients from both private doctors and larger centers, bearing a diagnosis of Cerebral Palsy, Behaviour Disorder, Mental Retardation, or Convulsive Disorder, we frequently see patients whose records would be impossible to record under average circumstances.

With the use of this drug, following a parallel pattern of a study recently published by Drs. Baird and Spiegel,[1] we have successfully recorded 281 cases which we could not have otherwise managed. This covers a group of children from age 6 weeks to 11 years.

The history of BULBOCAPNINE, a derivative of Corydalis Cava, a wild flower commonly referred to as Dutchman's Breeches, dates from the early 17th Century. It is described in the U. S. Dispensary 1947, has an Aporphine base and is soluble in distilled water, 1.40. A solution of 2.5 mg/kg, produces a cataleptic state, although preserving sensory and motor reactions in large measure.[2] In adult human subjects very large doses, 300 mg or more, have caused transient hypotension, vomiting, and shock.[3]

Although considerable study has been made of the site of action of this drug, no conclusive evidence has been derived other than the indications that the drug exerts a depressive effect on the Prosencephalon, Diencephalon, and Mesencephalon of the cat.[4,5,6] An appreciable diminution of voluntary activity of a motor nature was observed in laboratory animals, although electrical discharges of

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the Cortex are not significantly changed.[7] Somewhat more recent study by another group resulted in the observation of an increase in response of the Cortex to certain sensory stimuli, namely, light and sound, but still no definite conclusions as to the anatomical site of the drug's action could be drawn. (Passouant-Passouant Fountain & Cadilhac.

The use of this drug was first suggested as a possible source of sedation in the management of Paralysis Agitans and Post-encephalitic Behaviour Disorders. However, it was not of lasting value because of the short duration of its sedative effect, approximately 45 minutes, which, incidentally, is one factor which greatly enhances its value for EEG sedation.

In the study published by Drs. Baird and Spiegel, they noted that their subcutaneous injections were effective within 6 to 9 minutes, producing a progressive diminution of motor activity. Our experience has been that approximately 11 to 15 minutes are required to slow motor response. Similarly, a drowsiness was noted at 12 to 18 minutes in the original study, whereas in our laboratory 15 to 22 minutes is average for the appearance of drowsiness. It now seems pertinent to mention that we routinely exclude parents, family, or escort from our proceedings. Our technician greets the patient in the hospital lobby which allows for a few minutes acquaintance and evaluation prior to a actual activities in the laboratory which implement the recording. Following the drug injection, the technician routinely diverts the patient's attention with song or story in order to reassure and quiet the seldom tranquil subject. In keeping with the trend of the times, the technician takes the subject on a "Rocket Trip to the Moon and Outer Space," which interestingly enough is frequently the only subject of recall when the test has been completed.

Drowsiness and light sleep serve as excellent activation methods and usually supervene in approximately 22 minutes. The action of the drug persists for about 45 to 50 minutes, allowing ample time for the recording. The drug is prepared as a 2.5 per cent sterile solution in warm distilled water. The average dose given in our laboratory, based on 3.5 mg/kg of body weight is 1 to 3 cc. although we have given a dose as small as 0.5 cc and as large as 7.5 cc. On occasion a repetition of the dose has been necessitated either by overactivity or for some further procedure. The dose has been repeated 45 to 50 minutes later with good results. Other studies have reported some failures in obtaining good results, due primarily to inadequate dosage with the repeat dose causing vomiting.

We have been fortunate, for in our 281 cases we have had only two patients leave the laboratory with incomplete records. This resulted from extreme emotional upset in one case and severe retardation in the other. Both patients had frequent spontaneous arousals with an apparent fear response during the state of drowsiness. They never settled into a quiet enough state for EEG recording and were dismissed from the laboratory to return a week later. After excluding emotional factors, entirely satisfactory records were obtained the following week.

No significant local reaction at the site of injection has been noted except for very occasional redness. Some observers have reported swelling, but we have not encountered this reaction.[1] Systemically, we have noted some similar responses to those recorded by other observers, i.e., vomiting. We have had three such cases, although these were in children with palatal defects, and in children with a previous history of vomiting in stress situations. Other side effects seen by Drs. Baird and Spiegel, i.e., abdominal pain and cyanosis, have not been observed in our cases, although just prior to drowsiness, a marked circumoral pallor is invariably seen.

Arousal from this sedation has always been very prompt and is very often accompanied by a marked euphoric and affectionate response and occurs in the resistant patient as well as the calm one. Many times they ask to return to the moon or to stay with us, and a number of them have just wanted to be cuddled or talked to for a while.

To return to our major concern, that is, an EEG recording, relatively free from the artefact produced by drug activity, we have succeeded in deriving many of the same conclusions as those reached by Drs. Baird and Spiegel. We have had markedly reduced movement artefact, and our waking records are substantially the same as those in nonsedated cases. There is no evidence of alteration in the development or form of Alpha or Delta activity, either in frequency or amplitude. We, too, have noted a measurable reduction in Beta activity. Sleep patterns show no change from their usual forms of spindles and slow wave activity. No appreciable change occurs in the formation of abnormal wave patterns or discharges. The fast activity, so prominent in Barbiturate sedation, is absent from our records, except where rarely Barbiturates have been combined with BULCOCAPNINE, or where the routine medication of the patient is Barbiturates.

In summary, the drug has presented the opportunity for the reasonable management of patients whose adequate evaluation might otherwise have been entirely denied, and has relieved us of the somewhat obscuring artefact created by Barbiturates. It has the additional advantage of mild sedation with a conveniently short duration, permitting ready arousal. We have only one major hope for the future of BULBOCAPNINE and that is the thought that someone will be able to present the same adequate sedation in a less bulky form.

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Constipation in Infants and Children

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Delay or difficulty in defecation is a frequent complaint in pediatric practice. In children, as opposed to adults and the elderly, constipation may frequently subside of its own accord or respond to establishment of a regular routine, correction of obvious dietary errors, and reduction of family tensions. However, many cases exist, often those in whom constipation has become a symbol of intra-familial conflict, in whom there is a need for laxative therapy. The aim of treatment of such is not only to give temporary relief, but also to assist in re-establishing normal bowel habits.

The number of available laxatives is so great that a mnemonic device (Table I) is very helpful in grouping them. The drastic cathartics (category I . . . castor oil, etc.) have fallen into complete disuse, for there can be no excuse for irritating the immature intestinal tract. Most laxatives in common use fall into categories II, III and IV. Unfortunately, they often fail to bring about a satisfactory response. On the basis of the relative incidence of side reactions, a surface active agent (dioctyl sodium sulfosuccinate . . . category V) would appear to be the most suitable laxative for pediatric use; in our hands, however, its inocuousness has been fully matched by its ineffectiveness[1].

Next to the outmoded drastic cathartics, the most effective laxative agents are substances incorporating the anthraquinone structure. Until recently, these have been characterized, like other cathartics, by difficulty in getting children's dosage adjusted, with frequent over-dosage and uncomfortable reactions such as griping. Our attention has now been directed to a new preparation of this type, a senna derivative, which is assayed with far greater accuracy than heretofore possible, and reproducibly standardized, thus reducing the likelihood of accidental overdosage. It is purified in such a manner as to eliminate resin and other undesirable contaminants of the base material, resulting in a marked decrease in the incidence of side reactions. Being a mixture of three closely related active substances (sennosides), this preparation has no generic name but is known as Senokot**.

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** Supplied by the Medical Department of The Purdue Frederick Company, New York.

TABLE 1

SUMMARY OF COMMON CLASSES OF LAXATIVES

TYPE OF LAXATIVE	MODE OF ACTION				SIDE REACTIONS
	MUSCULAR IRRITATION	WATER RETENTION	NEUROMUSCULAR STIMULATION	FECAL SOFTENING	
I DRASTIC CATHARTICS	***				Griping Diarrhea
II SALINE CATHARTICS		**		*	Griping
III HYDROPHYLLIC COLLOIDS		***			Distention
IV ANTHRAQUINONE CATHARTICS			***		Griping
V DETERGENTS				***	None

Its pharmacology has been well described by Ryan[2] and by Gaddum[3]. It appears that Senokot has no irritant action whatever, in the conventional sense, on the intestinal mucosa, that it is broken down into an active hydrolysate in the colon, and that it acts by stimulating directly the ganglion cells of Auerbach's plexus in the colonic wall. For this reason, its action in adults[4] is reported to be almost indistinguishable from normal physiological defecation. Satisfactory results have indeed been reported in a preliminary study[5], on the use of Senokot in children, normal bowel action having been quickly restored in a majority of patients.

METHODS

The effectiveness of this preparation was evaluated in the present study in a total of fifty-two children, divided into three groups. These included 35 children between 2 and 14 years with functional constipation, 12 infants between 5 and 9 months of age with a spastic type of constipation, and 5 children in whom retention of stools was demonstrably on an emotional basis. The children had, as a minimum, a bowel frequency of less than one in 24 hours, and at least one of the following symptoms related to the constipation: hard stools, painful defecation, straining, abdominal distention or cramps. Anorexia and headache were also frequently present.

All children in these groups were carefully examined, including visual inspection of the rectum by means of the anoscope, and a detailed history was obtained in order to estimate the importance of emotional factors. These precautions must never be omitted when treatment of a constipated child is started or changed. While structural causes of constipation are but rarely encountered, psychological or environmental abnormalities are usually present and frequently become a significant factor in treatment.

RESULTS

A. *Functional Constipation*: Thirty-five children suffering from simple (functional) constipation were given a single dose of Senokot granules, consisting of one-half teaspoonful for children over, and one-quarter teaspoon for children under 60 lbs. During the following week, the parents were asked to chart daily the number of bowel movements and their average consistency.

Table II summarizes the average daily response of the 29 or 83% of the children in this group who demonstrated a very satisfactory degree of improvement, including relief of associated symptomatology, as opposed to the 6 who remained unimproved. These 29 all responded to a single dose of Senokot with a clear-cut laxative effect, increased frequency of bowel movements persisting, on the average, until the fourth day, and decreased fecal hardness persisting for at least a week. This tendency for the increased intestinal activity to carry over for several days is a most desirable effect.

TABLE II

SUMMARY OF RESULTS OF TREATMENT OF [illegible] WITH A SINGLE DOSE OF SENOKOT

NUMBER OF CHILDREN	RESULTS OF TREATMENT	BEFORE TREATMENT		DAYS AFTER TREATMENT						
		Frequency (per week)	Consistency (average)	1	2	3	4	5	6	7
				Frequency and average consistency						
29	Improved	3.2	S	4.6 S	2.0 S	0.8 S	0.5 S	0.4 S	0.6 S	0.7 S
6	Unimproved	2.8	S	1.2 H	0.7 S	0.7 S	0.2 S	0.3 S	0.3 S	0.8 S

Symbols for consistency of stools: S = soft, M = medium, H = hard

a Number of bowel movements.

In five children under three years of age, laxation was very vigorous on the first day, excessively so in two aged two years, one of whom had 14 bowel movements associated with flatus and discomfort during the first 12 hours, and the other, 9 bowel move-

ments during that period. This suggests that younger children (two years or less) should be treated with smaller initial amounts.

In these younger children, especially, Senokot proved to be unusually palatable for a laxative medication, so that its administration did not produce any traumatic experiences for the child. Details of the individual therapeutic results are given in Table III.

TABLE III

RESULTS OF TREATMENT OF THIRTY-FIVE CHILDREN WITH FUNCTIONAL CONSTIPATION WITH SINGLE DOSE OF SENOKOT

CASE	AGE	SEX	WEIGHT	BEFORE TREATMENT		DAYS AFTER TREATMENT							RESULT
				Frequency	Consistency	1	2	3	4	5	6	7	
	years		lbs.	per week	average	Frequency and average consistency							
1	2	F	26	3	H	9S	3S	1S	0	1M	0	1M	I
2	2	M	26	4	H	1M	3S	1M	0	0	1M	1M	I
3	2 1/2	F	29	4	"	5S	2M	1M	0	1H	0	1H	U
4	2 1/2	M	30	5	H	7S	3S	2S	2M	2M	2M	2M	I
5	3	M	34	5	"	9S	3S	1M	1M	0	1M	0	I
6	3	M	31	5	H	1H	1H	0	1H	0	1M	1H	I
7	3	F	33	3	M	5S	3S	1S	0	1M	0	0	U
8	3	M	33	3	H	1M	1M	1M	0	0	1M	0	U
9	3	"	27	3	H	5S	1S	0	1M	1M	1M	1M	I
10	4	F	36	2	H	1S	2S	0	1S	1M	0	0	I
11	4	F	35	4	H	3S	3S	1S	0	1M	1M	0	I
12	4	M	37	4	H	1L	6S	1S	0	1M	0	1M	I
13	5	M	40	5	H	4S	1S	0	0	0	1M	1M	I
14	6	F	43	3	H	3S	1M	1M	0	1M	1M	1M	I
15	6	F	44	3	H	6S	1S	1M	0	1H	0	1H	I
16	6	F	43	2	H	4S	1M	0	0	1M	1M	1M	I
17	7	M	53	2	H	3S	1S	0	1M	1H	0	1M	I
18	7	M	51	2	H	2S	1M	1M	0	1M	1M	1M	I
19	7	F	62	4	H	1M	0	1M	0	0	0	1M	U
20	7	F	51	1	H	4S	1S	1M	1L	0	1M	1M	I
21	8	M	64	5	H	2S	2S	1S	1M	0	1M	0	I
22	9	F	67	2	H	2S	1M	1M	0	1M	0	1M	I
23	9	M	60	3	H	3S	2S	2S	2M	0	0	1M	I
24	9	F	66	1	"	0	0	0	1M	0	0	0	U
25	9	F	66	5	H	4S	3S	1M	0	1M	1M	0	I
26	10	M	69	3	H	0	1M	0	0	1M	0	1M	U
27	11	F	78	2	M	2S	1S	0	1M	0	1H	0	I
28	12	F	98	2	H	2S	1M	1M	0	1H	0	1H	I
29	12	F	97	4	H	2S	1S	1M	1M	0	1M	0	I
30	12	F	102	3	H	2S	1M	1M	1M	0	1M	1M	I
31	13	M	106	2	H	0	0	1M	0	0	1H	0	U
32	13	F	101	3	M	1S	1M	1M	0	1M	1M	1M	I
33	13	F	89	3	H	3S	3S	0	1M	1M	0	1M	I
34	14	F	99	3	M	2S	1M	1M	1M	1H	0	0	I
35	14	M	117	3	H	2S	1S	1M	0	0	1M	0	I

I - Improved; U - Unimproved. Other symbols as in Table II.

The six children in whom the initial dosage of Senokot was ineffective were given successively increased amounts of this medication. At first, they received double the initial dose. This was effective in only two more (Table IV), and the remaining children were given four times the basic dose one week later. In spite of these increased dosage levels, no side effects or complaints of discomfort were encountered.

Two of these latter patients still failed to respond to treatment. Both had a long history of constipation accompanied by considerable distention. In the absence of other physical findings, there had seemed to be no reason to consider them as suffering from anything but severe functional constipation. In view of this lack of response to a neuroperistaltic agent, however, a radiological survey was performed and permitted a presumptive diagnosis of megacolon to be made. The two children were finally given eight times the basic dose of Senokot, but only one responded, whereas the other one (Table IV) was able to tolerate not only a single dose of four teaspoonfuls of Senokot but the same dose daily without either therapeutic or side effect.

TABLE IV

RESPONSE OF PREVIOUSLY REFRACTIVE PATIENTS TO INCREASING BASIC DOSE OF SENOKOT

CASE	AGE (Years)	DOSE (teaspoonfuls)	DAILY STOOL EVACUATION — Frequency and average consistency							PLATEAU
			1	2	3	4	5	6	7	
6	3	1/2	2H	1H	0	0	0	1H	0	0
8	3	1/2	4S	2H	1H	1H	1S	1H	1S	I
19	7	1	0	1H	0	0	0	0	1S	0
24	9	1	2	0	0	0	0	0	1S	0
26	10	1	3H	2H	1H	1H	1H	0	1H	I
31	13	1	0	0	0	1L	0	0	1H	0
6	3	1	3H	2H	1H	1H	1H	1H	0	I
19	7	2	2H	1H	1L	1H	1H	0	0	I
24	9	2	0	0	0	1L	0	0	0	0
31	13	2	0	0	1H	0	0	0	0	0
24	9	4	0	1H	0	0	0	0	0	0
31	13	4	3H	1H	1H	0	0	0	0	I

Symbols same as in Table III.

These findings revealed that about 90% of children with simple functional constipation will react to a basic dose of Senokot, 5% will require twice and 5% four times this amount. Children who fail to respond to four times the basic dose must be carefully re-evaluated for masked or overlooked organic pathology.

B. *Spastic Constipation (Infancy)*: In infants, constipation often tends to be of a characteristically spastic type, with much straining and crying which finally results in the passage of hard stools, almost the size and consistency of pebbles. Although this condition usually ceases spontaneously after a few months, the child often suffers from perirectal irritation, bleeding or infection while it persists, and the mother's emotional disturbance only rarely responds to reassurance.

Twelve children suffering from this complaint were given one-sixth level teaspoonful (about 0.5 gm.) of Senokot. Whereas prior to this, the children had had approximately one of these hard stools daily, there was complete relief from straining and fecal hardness for about 3–4 days in every case (Table V). Following this, the original condition returned. It therefore appears possible to control spastic constipation in infants for long periods of time by administering Senokot in this small dosage every fourth day.

TABLE V

RESULTS FROM SINGLE DOSES OF SENOKOT IN TWELVE INFANTS WITH CHARACTERISTICS OF THE SPASTIC TYPE

CASE	AGE (months)	SEX	WEIGHT (lbs.)	DAYS OF TREATMENT 1 2 3 4 5 6 7 Frequency and average consistency							RESULT
1	5	F	13 1/2	5D	3S	3S	1M	0	1S	1S	I
2	5	M	15 1/2	3S	2S	2S	0	0	1S	1S	I
3	6	F	15	4S	2S	2S	1S	0	1S	1S	I
4	7	F	15	5S	3S	1S	1L	1S	1L	1S	I
5	7	M	15 1/2	3S	2S	1M	0	1S	1S	1S	I
6	7	F	16 3/4	4S	1M	1M	1M	0	1S	1S	I
7	7	F	17 1/2	12S	2S	1M	1S	0	1S	1S	I
8	7	M	17 3/4	11S	3S	2S	2S	0	0	1S	I
9	8	M	15	3S	1M	1M	0	1S	1S	1S	I
10	8	M	15 1/2	6S	3S	1M	0	1L	0	1S	I
11	9	F	18	4S	1S	1M	0	0	1S	1S	I
12	9	M	21	3S	2S	0	1M	1S	0	*1S	I

C. *Constipation Associated with Emotional Disturbance:* As noted by Bakwin[6], the majority of constipated children do not impress one as emotionally disturbed, the bowel difficulty being an isolated symptom, although no doubt psychogenic in nature. Even in these cases, it is not certain whether the bowel difficulty causes the emotional upset or whether the emotional upset causes the constipation. In this series of 52 children, only 5 (10 per cent), all girls, gave evidence of emotional disturbance associated with stool retention. In each of these cases, the family situation had deteriorated to the degree that no bowel movement appeared spontaneously, some artificial stimulation such as suppositories or enemas being applied each time.

These children were placed on a unit dose of Senokot every third day, maintained for three weeks. The initial results (Table VI) were uniformly favorable, both objectively and subjectively. Following this first three-week period, the dose was reduced to one unit every week for a further three weeks, and then eliminated entirely. As a result of this gradual adjustment, three children remained much improved, with more frequent stools, less apprehen-

TABLE VI

THERAPEUTIC RESPONSE OF CHILDREN WITH PSYCHOGENIC CONSTIPATION

CASE	AGE	SEX	BEFORE TREATMENT		DURING TREATMENT		
			Frequency (per week)	Consistency	Frequency (per week)	Consistency	Symptoms
1	4	F	2	H	9	S	I
2	5	F	2	H	8	H	I
3	5	F	3/4	H	10	S	I
4	7	F	1	H	3	S	I
5	6	F	1 1/2	H	7	S	I

Symbols same as in Table III

sion and less emotional involvement; two others (cases *2* and *3*) reverted to their original condition. No side reactions of any kind were encountered. Considering the shortness and ease of therapy, this is a highly satisfactory result. Discussion with children and parents indicated that the experience of passing frequent stools painlessly and easily through use of Senokot had helped ease some of the emotional conflicts in these cases.

SUMMARY

1. Although simple functional constipation is believed to be psychogenic in almost all cases, associated emotional disturbances demonstrable without deep probing are present in a minority only. Laxative therapy is often called for as supportive therapy and should have the following desirable chacteristics: Lack of side reactions; effectiveness; uniformity of action; and a physiologic mechanism of activity.

2. Senokot, a purified and standardized senna derivative, was administered to 52 infants and children suffering from simple, psychogenic and spastic constipation. This medication proved to be more effective, far less prone to cause side reactions, and more palatable than other laxatives studied previously. It is long-acting, a single dose stimulating bowel activity and softening the stools for at least three days.

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Clinico-Pathological Conference

GEORGIA BAPTIST HOSPITAL, ATLANTA

JOSEPH YAMPOLSKY, M.D.,* *Chief of Pediatric Dept., Presiding*

DR. YAMPOLSKY: Today we are going to discuss a case of accidental poisoning due to ingestion of salicylate. This is a very common occurrence in young children, and approximately one-third of the cases of poisoning which are seen at the hospital consists of salicylate ingestion. I will ask Dr. Kepp to present the patient.

CASE PRESENTATION

DR. KEPP: This patient is a 1½ year old, white male, who was admitted to the Georgia Baptist Hospital with the chief complaint of fever, breathing hard and a "cold". The child's mother stated that the baby had a "cold" for the past week prior to admission associated with a mild degree of fever. Child was given 1¼ grs. of aspirin every 3 hours for fever, and the child did fairly well, the temperature spiking some, especially in the evening until three days prior to admission. At this time, his temperature became more elevated and seemed to stay around 102 and 103 degrees and from that time was given the same dose of aspirin every three hours around the clock. On the night of the day before admission, the child began to vomit especially after each dose of aspirin. The mother would give the child another aspirin following each regurgitation. The child was admitted to the hospital with a provisional diagnosis of salicylate poisoning. His past history has no bearing on the present admission.

Physical examination on admission revealed a fairly well developed, 1½ year old, white male, who weighed 25 lbs., pulse of 152, respirations 72 per minute. Temperature 100. The patient was somewhat agitated and Kussmaul type of breathing was present. The skin and mucous membranes were warm and dry. Bilateral otitis media was present.

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The lungs were clear, and the respirations were rapid. No murmurs or thrills were present. The child walked with a staggering gait and appeared to be ataxic in regard to his movements. The impression on admission was salicylism or possible diabetic acidosis.

On admission, the blood salicylate level was 80 mgs. %, CO_2 15.6 meq/l, chlorides 98.2 meq/l, sodium 150 meq/l, potassium 4.1 meq/l. The blood glucose was 127 megs. %. While the electrolyte reports were being prepared, the patient received approximately 200 ccs. of a solution containing 22 meq. of sodium and chloride per liter in 5 % Dextrose water, at which time the solution came out of the vein and attempts to re-start the intravenous fluids were unsuccessful. The patient was started on 500 ccs. of 2½% Glucose in distilled water as a subcutaneous clysis. As time progressed, the patient developed jerky movements of the extremities and by 12 hrs. after admission, the patient had lapsed into a coma without response to painful stimulation. Respirations at this time were quite rapid. Repeat electrolytes were chlorides 103 meq/l, potassium 3.6 meq/l, and sodium 128 meq/l. CO_2 was 14.3 meq/l. Blood salicylate level was 53 mgs. %. Since the child from a prior admission had bilateral cut-downs performed on the ankles, a brachial cut-down was done, and again a solution containing 22 meqs. of sodium and chloride was started with 125 mgs. of sodium bicarbonate. The child was also given 50 mgs. of Solu-Cortef IV at this time, and it was decided to proceed with an exchange transfusion due to the marked change in cerebral signs. The exchange transfusion was first started in a brachial cut-down area, but this was not practical and, therefore, a cut-down in the femoral region was performed using a # 15 catheter inserted through the saphenous vein into the femoral vein. The exchange performed was similar to the method used in exchanging the infants with erythroblastosis receiving approximately 500 ccs. of blood exchange and 50 ccs. as simple transfusion at the completion.

During the procedure the patient also received 10 ccs. of 10% Calcium Gluconate in divided doses IV. After the exchange the level of consciousness seemed somewhat higher and the patient would arouse to painful stimulation. Post exchange salicylate level was 42.8 mgs. %, and after a sufficient period of time to obtain more blood, a second exchange was performed using 500 ccs. of blood and at the end of this procedure, patient called for his mother and moved about considerably. During the next 24 hour-period following the second exchange, the child's condition varied consider-

ably from a conscious level to an unconscious level and since there was a possibility that there may have been another toxic substance other than salicylate present, another exchange was performed, at which time the pre-exchange level was 5 mgs. % for salicylate. 450 ccs. of blood were used in the third exchange and after the third exchange patient's condition rapidly improved. His level of consciousness became much higher leaving only a residual fine tremor of the extremities present. He was discharged 7 days from admission. He was doing very well without any signs of permanent damage. Ataxia had cleared. Studies of blood and urine at the state crime laboratory revealed no other common poisons present.

DR. YAMPOLSKY: Dr. Forbes, will you discuss the chemistry and physiology of the salicylates?

DR. FORBES, (Chief of Dept. of Pathology, Georgia Baptist Hospital): Salicylate poisoning, as Dr. Yampolsky has pointed out, is one of the more common poisonings in pediatric practice. Acetylsalicylic acid or aspirin is a relatively soluble and is quickly hydrolyzed in the stomach into its two radicals. The acetyl radical is easily handled and produces very little in the way of metabolic disturbances.

The salicylate acid radical however is a strong acid and when absorbed quickly combines itself with the bases of the blood. This immediately calls for a buffering action of the electrolytes and buffering system of the blood, and thereby carbon dioxide is reduced. The hyperventilation that results is one of the symptoms of this electrolyte imbalance.

A level of 10 mgs. % of salicylate is the blood level which usually produces tinnitus, vertigo, and early C.N.S. irritability. As higher levels are reached around 40 mgs. %, the convulsions, vomiting and hyperventilation are thought to be due to direct central nervous system stimulation of the salicylic acid. When 80 mgs. % is reached, there is usually unconsciousness with respiratory depression.

The fate of salicylic acid in the blood stream is absorption into the fatty tissues and parenchymal organs such as the liver and excretion through the kidney without metabolism other than conjugation with the bases of the blood. The sodium radical, which is the most common radical in the extra cellular fluid is excreted with the salicylic acid. Early in the course of salicylate poisoning, hyperventilation and vomiting can produce changes in the electrolytes,

which are only minor. This consists of CO_2 depression producing a respiratory alkalosis through hyperventilation. As time progresses and this is usually a fairly short period of time, excretion of the salicylic acid occurs through the kidneys with sodium attached, resulting in an acidosis. Usually there will be a reduced sodium level at the time acidosis is found. If the child has been dehydrated through vomiting, the reverse may be true and all electrolytes will be elevated. The sodium doesn't enter into the usual buffering mechanism with fixation to the salicylate portion. In the standard mode of therapy to combat this electrolyte imbalance, the use of sodium chloride provides both base and acid radicals allowing the patient themselves to adjust the buffering action. However, in very severe cases with prolonged acidity with low electrolytes, the actual use of sodium bicarbonate is recommended. This may also increase renal excretion of the salicylate.

A two fold jeopardy is produced when methyl salicylate is the toxic agent. This is oil of wintergreen and sometimes appeals to small children because of its sweet odor and taste. Very small amount of this, less than 1 oz. can produce death. The patients not only have the salicylate poisoning, but also have methyl radicals to contend with. This is just as if the child had ingested methyl alcohol. This is a readily absorbable substance. It is metabolized relatively rapid with carbohydrate oxidases to formaldehyde and then to formic acid. This is a permanent acid and combines again with the basic radicals. It also has the effect of direct intoxication upon the oxidase enzyme systems thereby blocking the utilization of carbohydrate. Methyl alcohol itself fixes to tissues very rapidly. It particularly has a propensity for brain and peripheral nerve myelin. This element is actually a solute for the methyl radical. The fatty tissues in subcutaneous tissue are also reservoirs for this. Methyl alcohol is not excreted in any appreciable amount in the urine. It is metabolized in the liver. The treatment for methyl alcohol poisoning must be abrupt, direct and drastic. The use of sodium bicarbonate in concentrations of 5 to 10% is life saving. If the patient has a very short onset after ingestion with profound acidosis and coma, we may also have convulsions. These patients are found to have large imbalances of electrolytes, the first being that of depression of carbon dioxide below detectable levels. This must be brought back quickly as well as the introduction of sodium radical to combat a very marked acidosis. Some of the problems of methyl alcohol poisoning or methyl radical poisoning are due to the fact

that so much of the radical is soluble in the fat and central nervous system.

After combating one episode of acidosis, you may, 2 hours later, have to repeat the same process because of the re-release and re-metabolism of the methyl alcohol that has been re-adsorbed from the depot fat and depot central nervous system. The methyl radical has some direct effect upon the nerve fibers, particularly the optic nerve; this is apparently the direct toxic effect of methyl radical producing optic atrophy and peripheral nerve atrophy. In comparing the two poisonings, one must realize that probably the methyl poisoning is the more serious of the two, but that treament for both salicylate poisoning and methyl alcohol poisoning is combating a profound acidosis even in the face of apparent alkalosis. Sodium bicarbonate is probably the drug of choice when this is the method to which you are limited.

DR. M. MCCLELLAN: In the post exchange period for erythroblastosis there is a rebound phenomenon of the serum bilirubin level. Would you expect to see a similar rebound in the salicylate level after exchange transfusion?

DR. FORBES: I would not ordinarily expect to see such a rebound phenomenon. The extra cellular fluid reservoir for the salicylates is a relatively small one, so the continued adsorption from the gastrointestinal tract of salicylates might be a more important factor than the reserve in the tissues.

DR. YAMPOLSKY: In regard to the use of extra corporeal dialysis, this process is limited to those centers where the procedure is available and trained personnel are present to handle a method of this kind. We feel that the simplicity of the exchange transfusion in the hands of most residents makes it easier to perform under the ordinary conditions. In our experience, we have had results which would indicate that the average hospital exchange transfusion should be used in preference to other methods in relieving intoxications due to salicylate poisoning.

Spritz et al[1] who summarized indications for dialysis or exchange, particularly salicylate intoxications, state that the coma, hyperpyrexia, seizures, delirium, and other manifestations of central nervous system involvement need to be corrected and that they feel that this kind of metabolic abnormalities cannot be easily managed by replacement therapy alone. We agree with them that the

concentration of salicylates in the blood cannot be held as a criteria for prognosis as to the toxicity of a particular patient. One follows ones' own judgment of the patient's condition rather than depending upon the exact blood level and blood concentration of salicylates alone.

DR. KEPP: In regard to the actual exchange itself; we have chosen to use the interval type (Diamond technique) since the house staff is trained in its use. There is evidence that a 40% replacement of patient's blood volume is the lowest effective level,[2] whereas a 90% replacement represents the highest practical value due to the larger donor blood volume required. Since our past experience with exchange replacements has been in erythroblastosis, the amount of donor blood is based upon this level. As a general rule, 75 ccs. per pound (165 ccs. per kilogram) will give close to a 90% effective replacement of the patient's blood. If the time required to perform a 90% exchange is not practical in the larger children, a smaller amount of donor blood, 19 ccs. per lb. (41 ccs. per kilogram) will give a 40% effective exchange. In using the smaller amounts of donor blood, the need for a repeat replacement will be more likely. Trossman and Alzofon have presented a formula to calculate data applicable to an exchange transfusion.[3]

DR. YAMPOLSKY: What are the indications for performing a repeat exchange transfusion in this condition?

DR. KEPP: A repeat replacement may be necessary depending upon several factors. (1) In exchanges that have been performed early especially after ingestion of methyl salicylate or large dose of aspirin, reaccumulation of blood salicylate levels may occur from the continued absorption from the gastrointestinal tract. (2) Individual sensitivity varies to the salicylates. (3) Age of the patient is a factor since infants may have toxic symptoms with the lower blood levels.[4] The decision for repeat exchange will have to be made on the severity of the symptoms, and the amount of metabolic disarrangement present after the prior exchange. To a certain degree, the post exchange or serial blood salicylate levels may be a helpful guide when correlated with the progress of the patient.

DR. FORBES: Dr. Kepp, do you think that interim salicylate levels during the exchange are of value in determining the amount of blood needed to produce the desired effect?

DR. KEPP: Yes, I believe that we all have seen the efficiency of

an exchange at times to be quite different from that expected. The decision to terminate an exchange earlier than calculated may be made if the blood salicylate level has dropped to a lower level, the acidosis is within an easily correctable range, and the patient is responding to the exchange. This may save the patient from being exposed to an unnecessary large amount of donor blood.

DR. YAMPOLSKY: On what basis would you choose between an exchange transfusion and correction of the electrolyte imbalance by intravenous fluid?

DR. KEPP: If with adequate fluid replacement, the patient continues to progress with untoward symptoms over a period of hours, it may be concluded that recovery will be prolonged unless blood replacement therapy is performed.

With ingestion of methyl salicylate (4 ml. = 2.7 gms. of acetylsalicylic acid?), or an exceeding large dose of acetylsalicylic acid that cannot be recovered by gastric lavage, a replacement may be started before the patient develops into severe acidosis.

DR. YAMPOLSKY: In conclusion, we would like to say that we have reported a case of salicylate poisoning in which exchange transfusion was used as the method of saving this patient's life. We can conclude that this is one more method that can be of much value in hands of people who are capable of using exchange transfusions in order to remove salicylate from the patients with salicylate poisoning.

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Authors' Summaries...

TARANTA, A.: Relation of Isolated Recurrences of Sydenham's Chorea to Preceding Streptococcal Infections. (New England Journal of Medicine 260:1204 June 11, 1959).

Sixty children who had had Sydenham's chorea, and were therefore susceptible to recurrences, were followed over a six-year period in two antistreptococcal prophylaxis clinics. A unique feature of these clinics was the routine periodic testing of throat cultures and streptococcal antibodies, permitting the detection and dating of even subclinical streptococcal infections with high reliability.

There were no recurrences of chorea in the 41 children who did not have streptococcal infections. Of 19 patients who had one or more streptococcal infections, 3 had recurrences of chorea. The recurrences were not preceded or accompanied by rheumatic polyarthritis or carditis, and their clinical onset was 3 to 6 months after the first immunologic evidence of streptococcal infection. They were not accompanied by a high erythrocyte sedimentation rate or a positive test for C-reactive protein, except in 1 patient, who had a second recurrence of chorea shortly after the first recurrence and an intervening streptococcal infection.

These data provide the first available evidence that Sydenham's chorea can follow infections with Group A streptococci by an interval longer than rheumatic polyarthritis and carditis, even in the absence of the latter manifestations and, indeed, in the absence of "rheumatic activity."

KLEIN, J. O.: Family Spread of Staphylococcal Disease Following a Nursery Outbreak. (New York State Journal of Medicine 60:861 March 15, 1960).

A survey of epidemic and nonepidemic infants was made at ten to fourteen months of life to determine the sequelae of a nursery outbreak of staphylococcal disease. Thirteen per cent of the infants had repeated furunculosis throughout the first year of life. Of the family contacts of infant cases, 12.6 per cent had developed a suppurative lesion during the ten months following the introduction of the infant into the household. Family contacts of infants without staphylococcal disease born during and following the epidemic had similar disease rates of 1.3 and 1.9 per cent. Thus a significant suppurative disease attack rate occurred only in family contacts of infant cases.

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Manner of Use:
After gently cleansing and drying the ear canal, Otamylon with Hydrocortisone (2 or 3 drops or moistened wick) is applied three or four times daily.

Supplied:
Combination package (15 cc.) with dropper: Otamylon and Hydrocortisone solutions readily mixed prior to dispensing.

Otamylon with Hydrocortisone is a clear, odorless, sterile, viscid liquid containing:

Sulfamylon™ HCl	5%
Benzocaine	5%
Hydrocortisone	0.02%
Anhydrous glycol q.s.	100

Otamylon and Sulfamylon (brand of mafenide), trademarks reg. U. S. Pat. Off.

Winthrop LABORATORIES
NEW YORK 18, N. Y.

How to win little friends and influence recovery

Tastefully tailored to the antibiotic needs of pediatric patients

new Cosa-Terrabon*

oxytetracycline with glucosamine

Delicious in taste: the appealing flavor of sweet, fresh fruit

Decisive in action: the well-tolerated broad-spectrum efficacy of Terramycin® with glucosamine

Preconstituted for uniform potency, efficacy, and taste-appeal from the first dose to the last.

Cosa-Terrabon Oral Suspension – 125 mg. oxytetracycline/5 cc., 2 oz. and 1 pint bottles

Cosa-Terrabon Pediatric Drops – 100 mg. oxytetracycline/1 cc., 10 cc. bottle with plastic calibrated dropper

*Trademark

Pfizer Laboratories, Div., Chas. Pfizer & Co., Inc., Brooklyn 6, N. Y.

Pfizer *Science for the world's well-being*™